

What is claimed is:

1. An antibody-conjugated enzyme, wherein the antibody recognizes a cell surface antigen on a tumor cell and wherein the enzyme activates a chemotherapeutic agent.
- 5 2. The antibody-conjugated enzyme of claim 1, wherein the enzyme is human deoxycytidine kinase.
3. The antibody-conjugated enzyme of claim 2, wherein the human deoxycytidine kinase has an amino acid sequence identified as SEQ ID NO: 1.
4. The antibody-conjugated enzyme of claim 1, wherein the enzyme is a
10 modified deoxycytidine kinase, wherein the modified deoxycytidine kinase has enhanced activity towards nucleoside analogs compared with wild type deoxycytidine kinase.
5. The antibody-conjugated enzyme of claim 4, wherein the modified deoxycytidine kinase has an amino acid sequence identified as SEQ ID NO: 5.
6. The antibody-conjugated enzyme of claim 1, wherein the antibody
15 recognizes CD33.
7. The antibody-conjugated enzyme of claim 6, wherein the antibody is HuM195.
8. The antibody-conjugated enzyme of claim 1, wherein the tumor cell is a leukemia blast cell.
- 20 9. The antibody-conjugated enzyme of claim 1, wherein the tumor cell is a prostate tumor cell, a breast tumor cell, an ovarian tumor cell, or a colon tumor cell.
10. The antibody-conjugated enzyme of claim 9, wherein the antibody is Herceptin and the tumor cell is a breast or ovarian tumor cell.

11. The antibody-conjugated enzyme of claim 9, wherein the enzyme is a modified deoxycytidine kinase, wherein the modified deoxycytidine kinase has enhanced activity towards nucleoside analogs compared with wild type deoxycytidine kinase.

12. The antibody-conjugated enzyme of claim 11, wherein the modified
5 deoxycytidine kinase has an amino acid sequence identified as SEQ ID NO: 5.

13. The antibody-conjugated enzyme of claim 9, wherein the antibody is immunologically specific for six-transmembrane epithelial antigen of the prostate, and the tumor cell is a prostate tumor cell.

14. The antibody-conjugated enzyme of claim 9, wherein the antibody is
10 immunologically specific for CC49, and the tumor cell is a colorectal tumor cell, an ovarian tumor cell, or a breast tumor cell.

15. The antibody-conjugated enzyme of claim 14, wherein the enzyme is a modified deoxycytidine kinase, wherein the modified deoxycytidine kinase has enhanced activity towards nucleoside analogs compared with wild type deoxycytidine kinase.

16. The antibody-conjugated enzyme of claim 15, wherein the modified
15 deoxycytidine kinase has an amino acid sequence identified as SEQ ID NO: 5.

17. A method of reducing, inhibiting or preventing proliferation of a tumor cell, comprising the step of contacting the tumor cell in the presence of a prodrug with an antibody-enzyme conjugate, wherein the enzyme converts the prodrug to an
20 antiproliferative drug, and wherein the antibody recognizes a cell surface antigen expressed at the cell surface of the tumor cell.

18. The method of claim 17, wherein the antibody-enzyme conjugate is internalized within the tumor cell and wherein the enzyme can activate the prodrug inside the tumor cell.

19. The method of claim 17, wherein the antibody-enzyme conjugate binds to
5 an antigen on the tumor cell and wherein the enzyme can activate the prodrug outside the tumor cell.

20. The method of claim 17, wherein the enzyme is human deoxycytidine kinase.

21. The method of claim 20, wherein the human deoxycytidine kinase has an
10 amino acid sequence identified as SEQ ID NO: 1.

22. The method of claim 17, wherein the enzyme is a modified deoxycytidine kinase, wherein the modified deoxycytidine kinase has enhanced activity towards nucleoside analogs compared with wild type deoxycytidine kinase.

23. The antibody-conjugated enzyme of claim 22, wherein the modified
15 deoxycytidine kinase has an amino acid sequence identified as SEQ ID NO: 5.

24. The method of claim 17, wherein the antibody recognizes CD33.

25. The method of claim 24, wherein the antibody is HuM195.

26. The method of claim 17, wherein the tumor cell is a leukemia blast cell.

27. The method of claim 17, wherein the tumor cell is a prostate tumor cell, a
20 breast tumor cell, an ovarian tumor cell, or a colon tumor cell.

28. The method of claim 27, wherein the antibody is Herceptin and the tumor cell is a breast or ovarian tumor cell.

29. The method of claim 28, wherein the enzyme is modified human deoxycytidine kinase having an amino acid sequence identified as SEQ ID NO. 5.

30. The method of claim 23, wherein the antibody is immunologically specific for six-transmembrane epithelial antigen of the prostate, and the tumor cell is a prostate
5 tumor cell.

31. The method of claim 26, wherein the enzyme is modified human deoxycytidine kinase having an amino acid sequence identified as SEQ ID NO. 5.

32. The method of claim 23, wherein the antibody is immunologically specific for CC49, and the tumor cell is a colorectal tumor cell, an ovarian tumor cell, or a breast
10 tumor cell.

33. The method of claim 27, wherein the enzyme is modified human deoxycytidine kinase having an enhanced activity towards nucleoside analogs compared with wild type deoxycytidine kinase.

34. The antibody-conjugated enzyme of claim 33, wherein the modified
15 deoxycytidine kinase has an amino acid sequence identified as SEQ ID NO: 5.

35. A method of reducing drug-resistance in a cancer patient comprising the steps of:

a. providing an enzyme conjugated to an antibody, wherein the enzyme activates a drug and wherein the antibody is specific for a cell surface antigen present
20 on a tumor cell;

b. administering the antibody-conjugated enzyme of step (a) to the patient;

and

c. administering the drug that is activated by the antibody-conjugated enzyme to the patient.

36. The method of claim 29, wherein the enzyme is a kinase and the drug is a chemotherapeutic agent.

5 37. The method of claim 30, wherein the kinase is deoxycytidine kinase and the chemotherapeutic agent is a nucleoside analog.

38. The method of claim 35, wherein the enzyme is human deoxycytidine kinase.

39. The antibody-conjugated enzyme of claim 38, wherein the human
10 deoxycytidine kinase has an amino acid sequence identified as SEQ ID NO: 1.

40. The antibody-conjugated enzyme of claim 35, wherein the enzyme is a modified deoxycytidine kinase, wherein the modified deoxycytidine kinase has enhanced activity towards nucleoside analogs compared with wild type deoxycytidine kinase.

41. The antibody-conjugated enzyme of claim 40, wherein the modified
15 deoxycytidine kinase has an amino acid sequence identified as SEQ ID NO: 5.

42. The method of claim 35, wherein the antibody is HuM195.

43. The method of claim 35, wherein the cancer is leukemia.

44. The method of claim 35, wherein the cancer is breast cancer, prostate cancer, ovarian cancer, or colon cancer.

20 45. The method of claim 35, wherein the antibody is Herceptin and the tumor cell is a breast or ovarian tumor cell.

46. The method of claim 45, wherein the enzyme is modified human deoxycytidine kinase having enhanced activity towards nucleoside analogs compared with wild type deoxycytidine kinase.

47. The antibody-conjugated enzyme of claim 46, wherein the modified
5 deoxycytidine kinase has an amino acid sequence identified as SEQ ID NO: 5.

48. The method of claim 35, wherein the antibody is immunologically specific for six-transmembrane epithelial antigen of the prostate, and the tumor cell is a prostate tumor cell.

49. The method of claim 48, wherein the enzyme is modified human
10 deoxycytidine kinase having enhanced activity towards nucleoside analogs compared with wild type deoxycytidine kinase.

50. The antibody-conjugated enzyme of claim 49, wherein the modified deoxycytidine kinase has an amino acid sequence identified as SEQ ID NO: 5.

51. The method of claim 35, wherein the antibody is immunologically specific
15 for CC49, and the tumor cell is a colorectal tumor cell, an ovarian tumor cell, or a breast tumor cell.

52. The method of claim 51, wherein the enzyme is modified human deoxycytidine kinase having enhanced activity towards nucleoside analogs compared with wild type deoxycytidine kinase.

53. The antibody-conjugated enzyme of claim 52, wherein the modified
20 deoxycytidine kinase has an amino acid sequence identified as SEQ ID NO: 5.

54. A method of treating a cancer patient comprising the steps of:

a. administering the antibody-conjugated enzyme of claim 1 to the patient;
and

b. administering a chemotherapeutic agent to the patient.

55. The method of claim 54, wherein the chemotherapeutic agent is a
5 nucleoside analog.

56. The method of claim 54, wherein the cancer is leukemia.

57. The method of claim 56, wherein the enzyme is a modified deoxycytidine
kinase having enhanced activity towards nucleoside analogs compared with wild type
deoxycytidine kinase.

10 58. The antibody-conjugated enzyme of claim 57, wherein the modified
deoxycytidine kinase has an amino acid sequence identified as SEQ ID NO: 5.

59. The method of claim 54, wherein the cancer is breast cancer, prostate
cancer, ovarian cancer, or colon cancer.

60. The method of claim 54, wherein the antibody is Herceptin and the cancer
15 a breast or ovarian cancer.

61. The method of claim 60, wherein the enzyme is modified human
deoxycytidine kinase having enhanced activity towards nucleoside analogs compared
with wild type deoxycytidine kinase.

62. The antibody-conjugated enzyme of claim 61, wherein the modified
20 deoxycytidine kinase has an amino acid sequence identified as SEQ ID NO: 5.

63. The method of claim 54, wherein the antibody is immunologically specific
for six-transmembrane epithelial antigen of the prostate, and the cancer is prostate cancer.

64. The method of claim 63, wherein the enzyme is modified human deoxycytidine kinase having enhanced activity towards nucleoside analogs compared with wild type deoxycytidine kinase.

65. The antibody-conjugated enzyme of claim 64, wherein the modified
5 deoxycytidine kinase has an amino acid sequence identified as SEQ ID NO: 5.

66. The method of claim 54, wherein the antibody is immunologically specific for CC49, and the cancer is colorectal cancer, ovarian cancer, or breast cancer.

67. The method of claim 66, wherein the enzyme is modified human deoxycytidine kinase having enhanced activity towards nucleoside analogs compared
10 with wild type deoxycytidine kinase.

68. The antibody-conjugated enzyme of claim 67, wherein the modified deoxycytidine kinase has an amino acid sequence identified as SEQ ID NO: 5.

69. A pharmaceutical composition comprising the antibody-conjugated enzyme of claim 1 and a pharmaceutical acceptable carrier.

15 70. A method of treating a cancer patient comprising the steps of:
a. administering the pharmaceutical composition of claim 69 to the patient;
and

b. administering a chemotherapeutic agent to the patient.

71. The method of claim 70, wherein the chemotherapeutic agent is a
20 nucleoside analog.

72. The method of claim 70, wherein the cancer is leukemia.

73. The method of claim 72, wherein the enzyme is a modified deoxycytidine kinase having enhanced activity towards nucleoside analogs compared with wild type deoxycytidine kinase.

74. The antibody-conjugated enzyme of claim 73, wherein the modified
5 deoxycytidine kinase has an amino acid sequence identified as SEQ ID NO: 5.

75. The method of claim 70, wherein the cancer is breast cancer, prostate cancer, ovarian cancer, or colon cancer.

76. The method of claim 75 wherein the antibody is Herceptin and the cancer
a breast or ovarian cancer.

10 77. The method of claim 76, wherein the enzyme is modified human deoxycytidine kinase having enhanced activity towards nucleoside analogs compared with wild type deoxycytidine kinase.

78. The antibody-conjugated enzyme of claim 77, wherein the modified deoxycytidine kinase has an amino acid sequence identified as SEQ ID NO: 5.

15 79. The method of claim 70, wherein the antibody is immunologically specific for six-transmembrane epithelial antigen of the prostate, and the cancer is prostate cancer.

80. The method of claim 79, wherein the enzyme is modified human deoxycytidine kinase having enhanced activity towards nucleoside analogs compared with wild type deoxycytidine kinase.

20 81. The antibody-conjugated enzyme of claim 80, wherein the modified deoxycytidine kinase has an amino acid sequence identified as SEQ ID NO: 5.

82. The method of claim 70, wherein the antibody is immunologically specific for CC49, and the cancer is colorectal cancer, ovarian cancer, or breast cancer.

83. The method of claim 82, wherein the enzyme is modified human deoxycytidine kinase having enhanced activity towards nucleoside analogs compared with wild type deoxycytidine kinase.

84. The antibody-conjugated enzyme of claim 83, wherein the modified
5 deoxycytidine kinase has an amino acid sequence identified as SEQ ID NO: 5.

85. A method of increasing the efficacy of a chemotherapeutic agent in a cancer patient, the method comprising the steps of:

a. providing an enzyme conjugated to an antibody, wherein the enzyme activates the chemotherapeutic agent and wherein the antibody is specific for a cell
10 surface antigen present on a tumor cell;

b. administering the antibody-conjugated enzyme of step (a) to the patient;
and

c. administering the chemotherapeutic agent that is activated by the antibody-conjugated enzyme to the patient.

15 86. The method of claim 85, wherein the enzyme is a kinase and the chemotherapeutic agent is a nucleoside analog.

87. The antibody-conjugated enzyme of claim 85, wherein the enzyme is human deoxycytidine kinase.

88. The antibody-conjugated enzyme of claim 87, wherein the human
20 deoxycytidine kinase has an amino acid sequence identified as SEQ ID NO: 1.

89. The antibody-conjugated enzyme of claim 85, wherein the enzyme is a modified deoxycytidine kinase, wherein the modified deoxycytidine kinase has enhanced activity towards nucleoside analogs compared with wild type deoxycytidine kinase.

90. The antibody-conjugated enzyme of claim 89, wherein the modified deoxycytidine kinase has an amino acid sequence identified as SEQ ID NO: 5.

91. The method of claim 85, wherein the antibody is HuM195.

92. The method of claim 85, wherein the cancer is leukemia.

5 93. The method of claim 85, wherein the enzyme is a modified deoxycytidine kinase having enhanced activity towards nucleoside analogs compared with wild type deoxycytidine kinase.

94. The antibody-conjugated enzyme of claim 93, wherein the modified deoxycytidine kinase has an amino acid sequence identified as SEQ ID NO: 5.

10 95. The method of claim 85, wherein the cancer is breast cancer, prostate cancer, ovarian cancer, or colon cancer.

96. The method of claim 85, wherein the antibody is Herceptin and the cancer a breast or ovarian cancer.

15 97. The method of claim 96, wherein the enzyme is modified human deoxycytidine kinase having enhanced activity towards nucleoside analogs compared with wild type deoxycytidine kinase.

98. The antibody-conjugated enzyme of claim 97, wherein the modified deoxycytidine kinase has an amino acid sequence identified as SEQ ID NO: 5.

20 99. The method of claim 85, wherein the antibody is immunologically specific for six-transmembrane epithelial antigen of the prostate, and the cancer is prostate cancer.

100. The method of claim 99, wherein the enzyme is modified human deoxycytidine kinase having enhanced activity towards nucleoside analogs compared with wild type deoxycytidine kinase.

101. The antibody-conjugated enzyme of claim 100, wherein the modified deoxycytidine kinase has an amino acid sequence identified as SEQ ID NO: 5.

102. The method of claim 85, wherein the antibody is immunologically specific for CC49, and the cancer is colorectal cancer, ovarian cancer, or breast cancer.

5 103. The method of claim 102, wherein the enzyme is modified human deoxycytidine kinase having enhanced activity towards nucleoside analogs compared with wild type deoxycytidine kinase.

104. The antibody-conjugated enzyme of claim 104, wherein the modified deoxycytidine kinase has an amino acid sequence identified as SEQ ID NO: 5.

10 105. A method of treating a cancer patient comprising the steps of:

a. providing a kinase conjugated to an antibody, wherein the kinase activates a chemotherapeutic agent and wherein the antibody is specific for a cell surface antigen present on a tumor cell;

b. administering the antibody-conjugated kinase of step (a) to the patient; and

15 c. administering the chemotherapeutic agent to the patient.

106. The method of claim 105, wherein the kinase is deoxycytidine kinase and the chemotherapeutic agent is a nucleoside analog.

107. The antibody-conjugated enzyme of claim 106, wherein the enzyme is human deoxycytidine kinase.

20 108. The antibody-conjugated enzyme of claim 107, wherein the human deoxycytidine kinase has an amino acid sequence identified as SEQ ID NO: 1.

109. The method of claim 105, wherein the deoxycytidine kinase is a modified deoxycytidine kinase having enhanced activity towards nucleoside analogs compared with wild type deoxycytidine kinase.

110. The antibody-conjugated enzyme of claim 109, wherein the modified
5 deoxycytidine kinase has an amino acid sequence identified as SEQ ID NO: 5.

111. The method of claim 105, wherein the antibody is HuM195.

112. The method of claim 105, wherein the cancer is leukemia.

113. The method of claim 112, wherein the enzyme is a modified
10 deoxycytidine kinase having enhanced activity towards nucleoside analogs compared with wild type deoxycytidine kinase.

114. The antibody-conjugated enzyme of claim 113, wherein the modified deoxycytidine kinase has an amino acid sequence identified as SEQ ID NO: 5.

115. The method of claim 105, wherein the cancer is breast cancer, prostate cancer, ovarian cancer, or colon cancer.

116. The method of claim 105 wherein the antibody is Herceptin and the cancer
15 a breast or ovarian cancer.

117. The method of claim 116, wherein the enzyme is modified human deoxycytidine kinase having enhanced activity towards nucleoside analogs compared with wild type deoxycytidine kinase.

118. The antibody-conjugated enzyme of claim 117, wherein the modified
20 deoxycytidine kinase has an amino acid sequence identified as SEQ ID NO: 5.

119. The method of claim 105, wherein the antibody is immunologically specific for six-transmembrane epithelial antigen of the prostate, and the cancer is prostate cancer.

120. The method of claim 119, wherein the enzyme is modified human
5 deoxycytidine kinase having enhanced activity towards nucleoside analogs compared with wild type deoxycytidine kinase.

121. The antibody-conjugated enzyme of claim 120, wherein the modified deoxycytidine kinase has an amino acid sequence identified as SEQ ID NO: 5.

122. The method of claim 105, wherein the antibody is immunologically
10 specific for CC49, and the cancer is colorectal cancer, ovarian cancer, or breast cancer.

123. The method of claim 122, wherein the enzyme is modified human deoxycytidine kinase having enhanced activity towards nucleoside analogs compared with wild type deoxycytidine kinase.

124. The antibody-conjugated enzyme of claim 123, wherein the modified
15 deoxycytidine kinase has an amino acid sequence identified as SEQ ID NO: 5.

125. A method of overcoming chemotherapeutic drug resistance in a cancer patient, comprising the steps of:

- a. providing a enzyme conjugated to an antibody, wherein the enzyme activates a chemotherapeutic agent and wherein the antibody is specific for a cell surface
20 antigen present on a tumor cell;
- b. administering the antibody-conjugated enzyme of step (a) to the patient;
- and
- c. administering the chemotherapeutic agent to the patient.

126. The method of claim 125, wherein the enzyme is a kinase.

127. The method of claim 126, wherein the kinase is deoxycytidine kinase and the chemotherapeutic agent is a nucleoside analog.

128. The antibody-conjugated enzyme of claim 126, wherein the deoxycytidine
5 kinase has an amino acid sequence identified as SEQ ID NO: 1.

129. The antibody-conjugated enzyme of claim 125, wherein the enzyme is a modified deoxycytidine kinase, wherein the modified deoxycytidine kinase has enhanced activity towards nucleoside analogs compared with wild type deoxycytidine kinase.

130. The antibody-conjugated enzyme of claim 129, wherein the modified
10 deoxycytidine kinase has an amino acid sequence identified as SEQ ID NO: 5.

131. The method of claim 129, wherein the antibody is HuM195.

132. The method of claim 129, wherein the cancer is leukemia.

133. The method of claim 132, wherein the enzyme is a modified deoxycytidine kinase, having enhanced activity towards nucleoside analogs compared
15 with wild type deoxycytidine kinase.

134. The antibody-conjugated enzyme of claim 133, wherein the modified deoxycytidine kinase has an amino acid sequence identified as SEQ ID NO: 5.

135. The method of claim 129, wherein the cancer is breast cancer, prostate cancer, ovarian cancer, or colon cancer.

20 136. The method of claim 129 wherein the antibody is Herceptin and the cancer a breast or ovarian cancer.

137. The method of claim 136, wherein the enzyme is modified human deoxycytidine kinase having enhanced activity towards nucleoside analogs compared with wild type deoxycytidine kinase.

138. The antibody-conjugated enzyme of claim 137, wherein the modified
5 deoxycytidine kinase has an amino acid sequence identified as SEQ ID NO: 5.

139. The method of claim 129, wherein the antibody is immunologically specific for six-transmembrane epithelial antigen of the prostate, and the cancer is prostate cancer.

140. The method of claim 139, wherein the enzyme is modified human
10 deoxycytidine kinase having enhanced activity towards nucleoside analogs compared with wild type deoxycytidine kinase.

141. The antibody-conjugated enzyme of claim 140, wherein the modified deoxycytidine kinase has an amino acid sequence identified as SEQ ID NO: 5.

142. The method of claim 129, wherein the antibody is immunologically
15 specific for CC49, and the cancer is colorectal cancer, ovarian cancer, or breast cancer.

143. The method of claim 142, wherein the enzyme is modified human deoxycytidine kinase having enhanced activity towards nucleoside analogs compared with wild type deoxycytidine kinase.

144. The antibody-conjugated enzyme of claim 133, wherein the modified
20 deoxycytidine kinase has an amino acid sequence identified as SEQ ID NO: 5.

145. A method of overcoming chemotherapeutic drug resistance in a tumor cell, comprising the steps of:

a. providing a enzyme conjugated to an antibody, wherein the enzyme activates a chemotherapeutic agent and wherein the antibody is specific for a cell surface antigen present on a tumor cell; and

b. contacting the tumor cell with the antibody-conjugated enzyme of step (a)
5 to the patient.

146. The method of claim 145, wherein the enzyme is a kinase.

147. The method of claim 146, wherein the kinase is deoxycytidine kinase and the chemotherapeutic agent is a nucleoside analog.

148. The antibody-conjugated enzyme of claim 147, wherein the deoxycytidine
10 kinase has an amino acid sequence identified as SEQ ID NO: 1.

149. The antibody-conjugated enzyme of claim 145, wherein the enzyme is a modified deoxycytidine kinase, wherein the modified deoxycytidine kinase has enhanced activity towards nucleoside analogs compared with wild type deoxycytidine kinase.

150. The antibody-conjugated enzyme of claim 149, wherein the modified
15 deoxycytidine kinase has an amino acid sequence identified as SEQ ID NO: 5.

151. The method of claim 145, wherein the antibody is HuM195.

152. The method of claim 145, wherein the tumor cell is a leukemia blast cell.

153. The method of claim 152, wherein the enzyme is a modified deoxycytidine kinase, having enhanced activity towards nucleoside analogs compared
20 with wild type deoxycytidine kinase.

154. The antibody-conjugated enzyme of claim 153, wherein the modified deoxycytidine kinase has an amino acid sequence identified as SEQ ID NO: 5

155. The method of claim 145, wherein the tumor cell is a breast, prostate, colon, or ovarian.

156. The method of claim 145, wherein the antibody is Herceptin and the tumor cell is a breast or ovarian tumor cell.

5 157. The method of claim 156, wherein the enzyme is modified human deoxycytidine kinase having enhanced activity towards nucleoside analogs compared with wild type deoxycytidine kinase.

158. The antibody-conjugated enzyme of claim 157, wherein the modified deoxycytidine kinase has an amino acid sequence identified as SEQ ID NO: 5.

10 159. The method of claim 145, wherein the antibody is immunologically specific for six-transmembrane epithelial antigen of the prostate, and the tumor cell is a prostate tumor cell.

160. The method of claim 159, wherein the enzyme is modified human deoxycytidine kinase having enhanced activity towards nucleoside analogs compared
15 with wild type deoxycytidine kinase.

161. The antibody-conjugated enzyme of claim 160, wherein the modified deoxycytidine kinase has an amino acid sequence identified as SEQ ID NO: 5.

162. The method of claim 145, wherein the antibody is immunologically specific for CC49, and the tumor cell is a colorectal tumor cell, an ovarian tumor cell, or
20 a breast tumor cell.

163. The method of claim 162, wherein the enzyme is modified human deoxycytidine kinase having enhanced activity towards nucleoside analogs compared with wild type deoxycytidine kinase.

164. The antibody-conjugated enzyme of claim 163, wherein the modified deoxycytidine kinase has an amino acid sequence identified as SEQ ID NO: 5.

165. A modified deoxycytidine kinase having an amino acid sequence identified as SEQ ID NO. 5.

5 166. An isolated polynucleotide encoding the modified deoxycytidine kinase of claim 165.

167. An expression vector comprising the polynucleotide of claim 166.

168. A host cell comprising the expression vector of claim 167.

169. A method of making a modified deoxycytidine kinase having an amino
10 acid sequence identified as SEQ ID NO. 5, the method comprising the steps of:

a) culturing the host cell of claim 168 under conditions whereby the kinase is expressed; and

b) purifying the antagonist from the host cell culture.